MicroPET: High Resolution Molecular Imaging In Vivo with Positron Emission Tomography

Simon R. Cherry, Ph.D.
Crump Institute for Biological Imaging,
UCLA School of Medicine, Los Angeles, CA

Positron Emission Tomography (PET) allows the temporal and spatial distribution of positron-labeled compounds to be determined in vivo. PET has been used for over 20 years as a tool for studying biological processes in the human and is finding increasing use as a clinical tool, particularly in oncology. Positron-emitting isotopes of carbon, nitrogen and oxygen are available, allowing many compounds of biological significance to be tagged with a positron-emitter, without altering their biochemical properties. A positron-emitting isotope of fluorine is also widely used, as it can be used to replace OH groups with minimal effects on the biological activity of the compound. Several hundreds of different compounds have now been synthesized with positron-emitting labels, allowing a wide range of processes, including glucose metabolism, protein synthesis, neurotransmitter chemistry and gene expression to be measured. An important feature of PET is that the sensitivity of radioisotope detection allows virtually massless quantities of the compound to be introduced for imaging – typical concentrations that can be visualized in PET images are in the nanomolar to picomolar range, although in theory, even lower concentrations can be detected and quantified under ideal conditions.

We are interested in trying to develop PET as a fundamental tool in modern biology. In particular, PET offers the possibility of repeatedly studying a wide range of biological processes in living laboratory animals such as mice and rats, thus giving the biologist a unique tool for studying the increasingly rich repertoire of animal models reflecting human disease and injury. The ability to study an animal more than once, allows each animal to serve as its own control (improving the statistical power of the study) and allows interventional strategies to be followed over time. Furthermore, volumetric data, often from the entire animal, showing the entire kinetic time course of the labeled compound is available within minutes of the end of the study for analysis. Despite these apparent advantages, the challenges are considerable. The resolution of human PET scanners, is at best 64mm^3, which is insufficient for the majority of applications in the mouse and rat. PET scanners are large and expensive devices, not well suited for use in a biology lab. The goal of our laboratory has therefore been to develop very high resolution, compact, PET systems, suitable for small animal imaging.

MicroPET is a prototype small animal PET scanner. It consists of a ring of 30 position sensitive scintillation detectors, each consisting of 64 elements of lutetium oxyorthosilicate scintillator coupled via optical fibers to a multichannel photomultiplier tube. The scanner has an aperture of 17 cm and a volumetric field of view of 10 cm (transaxially) by 1.8 cm (axially). The reconstructed image resolution is 1.8 mm and is isotropic, yielding a volumetric resolution of 6 mm^3. The absolute sensitivity of the

device is 200 cps/microCi at the center of the field of view. Over 1100 animal studies have been performed on this system, in a wide range of applications including studies of gene expression, brain injury, antibodies, myocardial perfusion and metabolism, the dopaminergic system and brain plasticity during development. Examples will be presented highlighting both the strengths and limitations of the use of PET in small animal studies.

We are currently in the process of producing a 2^{nd} generation microPET, which is projected to have 1 mm^3 resolution and will be a benchtop device. We are also exploring the possibility of combined PET/MRI and PET/CT systems for small animal imaging to provide high resolution anatomical and molecular imaging in a single setting.